UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/720,006	12/19/2000	Johann Karl	05-042	5872

20306 7590 02/15/2007

MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 S. WACKER DRIVE
32ND FLOOR
CHICAGO, IL 60606

EXAMINER	
FOSTER, CHRISTINE E	
ART UNIT	**PAPER NUMBER**
1641	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/15/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/720,006	KARL ET AL.	
	Examiner	Art Unit	
	Christine Foster	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-52,73 and 74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-52,73 and 74* is/are rejected.

7)☒ Claim(s) *44* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's amendment, filed 11/29/06, is acknowledged and has been entered. Claims 44-45, 48-49, 51-52, and 73-74 were amended. Claims 44-52 and 73-74 are currently pending and under examination.

Applicant is reminded of the proper format for amendments to the claims. All claims being currently amended must be presented with markings to indicate the changes that have been made relative to the immediate prior version. See MPEP 714.

Specifically, the examiner notes that in claim 44, the word "are" has apparently been deleted in line 4 of part (b); however there are no markings to indicate this change.

Objections/Rejections Withdrawn

2. The objections to claims 44-55 have been obviated by the amendments.

3. The rejections of claims 44-52 and 73-74 under 35 USC 112, 1st paragraph (new matter) regarding the recitation of "multicomponent" detection of two "analyte-specific components" has been withdrawn in response to the amendments to recite "multiepitope" detection of two "epitopes".

4. The rejection of claim 49 under 35 USC 112, 1st paragraph (new matter) regarding the recitation of "an analyte bound to the first test area is not simultaneously bound to the second test area" has been withdrawn in response to the amendments removing this phrase.

5. The rejections of claims 48 and 52 under 35 USC 112, 1st paragraph (new matter) regarding the recitation of a "signal-generating reagent" are withdrawn in response to the amendments removing this phrase.

6. The rejection of claim 74 under 35 USC 112, 1st paragraph (new matter) regarding the recitation of a "test area-specific cut-off" is withdrawn in response to Applicant's arguments (see p. 8), specifically Applicant's arguments that the limitation is supported in the disclosure at p. 21.

7. The rejections under 112, 2nd paragraph not reiterated below have been obviated by the amendments.

8. The rejections of claims 44, 47, 49, 51, and 74 under 35 U.S.C. 102(e) as being anticipated by Linsley et al., and of claims 46, 48, 50 and 52 under 35 U.S.C. 103(a) as being unpatentable over Linsley et al. in view of Ekins et al., are withdrawn in response to the amendments to claims 44, 49, and 51 to recite that a single application of the sample simultaneously contacts the first and second test areas and in response to Applicant's persuasive arguments (see p. 10). Since it is not clear from the reference whether the receptors in Linsley et al. were coated onto different wells of the same microtiter plate (as argued by the examiner) or alternatively onto different wells of multiple plates (as argued by Applicant), the rejections have been withdrawn.

9. The rejections of claims 44-46, 48, and 73 under 35 USC 103(a) as being unpatentable over Ekins in view of Schonbrunner are withdrawn in response to the amendments to claim 44 to recite that "a single application of the sample is contacted with the solid phase, and wherein the single application of the sample simultaneously contacts the first and second spatially separate test areas".

Information Disclosure Statement

Applicant requests that the examiner consider the Information Disclosure Statements mailed 5/22/01 and 9/13/05. The Information Disclosure Statements Applicant refers to were previously considered by the Office as indicated by the signed and initialed copies provided with the Office actions mailed on 12/3/02 and on 5/30/06, respectively.

Claim Objections

10. Claim 44 is objected to because of the following informalities:

The claim appears to have a period at the end of line 4 of part (c) rather than a comma or semicolon.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 44-52 and 73-74 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a new matter rejection.*

13. Claim 44 has been amended to recite "separately determining presence or amount of the signal generating group bound to the first **or** test areas" (see part (c) of claim 44, emphasis added); the claim previously recited determining the signal generating group bound to the first "**and**" second test areas. This change from "and" to "or" changes the scope of the claim, since it now means that the presence of the signal generating group is only determined in one of the test areas, and not both.

Applicant's reply indicates that support may be found in the specification at p. 6, second full paragraph and in Example 2 (Reply, p. 5-6).

Page 6, the second full paragraph discloses:

> **If a positive test result is obtained on one or several, and in some cases on at least two test areas, this is assessed as indicating the presence of the analyte in the sample.**

This passage does not provide support for "separately determining presence or amount of the signal generating group bound to the first **or** test areas" as in claim 44 because the passage relates to the *results* of the detection method, i.e., whether a positive result is *obtained* in one or more test areas. By contrast, step (c) of claim 44 calls out an active method step in which the presence or amount of the signal generating group is determined in only one of the test areas.

One skilled in the art would not envisage possession of methods of detecting signal in only one test area by the above disclosure, since in order to determine if a positive result was found in one or several of the test areas, the signal would have to be actually determined in all of the areas. This is also seen in Example 2 (see the table on p. 25), where the signal was detected in each of the test areas (represented by the different vertical columns p24, gp41 peptide, etc.).

No support could be found for determining the presence or amount of the signal in only one of the test areas, i.e., in either the first or second test area.

14. The amendments to claim 74 changing "and" to "or" as above also introduce new matter for the following reasons. The claim now recites that the presence or amount of the analyte in the sample is determined by the presence or amount of the signal generating group "bound to the first **or** second test areas *via the at least two epitopes*". Thus, the claim now refers to "the signal generating group bound to the first test area via the at least two epitopes" and "the signal generating group bound to the second test area via the at least two epitopes". Previously, the claim recited "the signal generating group bound to the first **and** second test areas via the at least two analyte-specific components", which implied that in the first test area, the signal generating group may be bound via one analyte-specific components, while in the second test area, the signal generating group was bound via a different analyte-specific component. This conveys a different meaning and a different scope from what is now claimed.

The amended claim now suggests that the signal generating group is bound "via at least two epitopes" in either of the test areas. However, there is no disclosure of the signal generating group being bound "via at least two epitopes" to any test area. There is no disclosure of signal generating groups that can bind to *multiple* epitopes, as implied by the current claim language. The amended claim language introduces new concepts never disclosed in the original specification or claims—for example, the claim could be interpreted to mean that the signal generating group binds via the "first" and "second" epitopes that are mentioned in claim 44. However, there is no disclosure of such a

scenario or even a suggestion of how this might be done. Since the first and second epitopes are bound by the immobilized first and second receptors, respectively, the epitopes would not be accessible for binding by the signal generating group.

15. Claims 48 and 51-52 as amended now recite that the detection reagent comprises "one or more of a third receptor that binds specifically with the epitope(s) of the analyte and a signal-generating group which is either directly bound to the third receptor or which is a universal detection reagent comprising labeled latex particles which binds to the third receptor".

Applicant's reply states that support for the amendments may be found at Example 1, page 23, lines 10-19, page 5, lines 20-24, page 9, lines 6-29, and page 13, lines 23-26.

The amended claims represent a departure from the specification and claims as originally filed because support could not be found where indicated for "one or more of a third receptor that binds specifically ***with the epitope(s)*** **of the analyte**" (emphasis added). The specification states that free analyte-specific receptors may be used in addition to the immobilized receptors (see p. 5). Thus, although the specification states that the free or third receptors may be specific to the analyte, there is no disclosure that they bind specifically with *the epitope(s)* of the analyte as currently claimed.

The examiner notes that is not entirely clear what "the epitope(s) of the analyte" refer back to since claims 44, 49, and 51 refer to "at least two epitopes" as well as to "first" and "second" epitopes (see rejection under 112, 2nd paragraph below). However, the claims would reasonably encompass situations where "the epitope(s) of the analyte"

refer back to the "first" and "second" epitopes. This would mean that the third receptor binds specifically with the first and second epitopes of the analyte *to which the first and second receptors bind.* The specification lacks written description for such a scenario. Nowhere is it mentioned that the free or third receptor binds to the same epitope(s) as the immobilized receptors. It would seem that such a method and kit would actually be inoperable in the sandwich assay formats disclosed, since the epitopes on the analyte that are bound by the first and second receptors would be inaccessible to the third or more receptors.

The specification does not provide blaze marks nor direction for the instant methods encompassing the above-mentioned limitations, as currently recited. The instant claims now recite limitations that were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

16. Claims 44 and 49 now recite that "a single application of the sample is contacted with the solid phase" and that "the single application of the sample simultaneously contacts the first and second spatially separate test areas", which represents a departure from the specification and claims as originally filed. Applicant's reply indicates that support may be found in the specification at p. 23, lines 5-9, which discloses that:

> **In this test procedure 30 µl sample diluted in a ratio of 1:1 with sample buffer is pipetted onto the support provided with test areas and incubated for 20 minutes while shaking at room temperature.**

The above passage fails to provide blaze marks or direction for the instant methods encompassing the above-mentioned limitations, as currently recited. There is no mention in the passage above that the first and second test areas are simultaneously contacted with the sample as claimed, and Applicant has not established that pipetting onto the support would inherently, i.e. *necessarily and always,* result in "simultaneous" contacting of the sample with the first and second test areas. Note that in the broadest reasonable interpretation, "simultaneously" contacting would mean at the exact same time; even in a solid support where the test areas are close to each other, for example as in the printed array in the above example, pipetting a single aliquot onto the surface of the array would not necessarily and always contact all of the array spots simultaneously, since the leading edge of a drop pipetted as above might first contact one array spot before wetting others.

Furthermore, the disclosure of *pipetting 30 μl of sample diluted 1:1 with sample buffer* does not fully support the currently claimed limitation of contacting a "single application" of sample with the solid phase. Applicant's reliance on generic disclosure (contacting the sample with the solid phase) and possibly a single or limited species (pipetting 30 μl of sample diluted 1:1 with sample buffer) does not provide sufficient direction and guidance to the features currently claimed (contacting a single application of sample simultaneously with the first and second test areas on the solid phase). It is noted that a generic or a sub-generic disclosure cannot support a species unless the species is specifically described. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

17. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claims 44-52 and 73-74 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

19. Claim 44 recites "***separately*** determining presence or amount of the signal generating group bound to the first ***or*** the second test areas" in part (c) (emphasis added). The claim is indefinite because it now refers to determining signal in either the first or the second test areas. Since only one test area is now being determined, it is unclear what the recitation of "separately" determining refers to. It is unclear how a signal from a single test area could be determined "separately"—separately from what?

20. Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "**analyte**" in claims 44-52 and 73-74 is apparently used by the claim to mean "**a heterogeneous population of different molecules**", while the accepted meaning is "**a single molecule.**" The term is indefinite because the specification does not clearly redefine the term.

Amended claims 44, 49, and 51 recite "multiepitope" detection of "**an analyte.**" The recitation of "an analyte" implies that a single species is being detected. Claim 45

also refers to "the analyte". However, new claim 73 recites that the analyte may comprise "two different...antigens, two different...antibodies or at least one...antigen and one...antibody."

The specification does not clearly define the term "analyte". The specification at p. 5, the last paragraph suggests that the analyte may be a homogeneous or heterogeneous population. However, this exemplification does not represent a limiting definition of the term "analyte".

An "analyte" has been defined as "**a molecule** that is targeted by a particular quantification method" (Macmillan Dictionary of Toxicology (1999). Retrieved 16 May 2006, from xreferplus. http://www.xreferplus.com/entry/972936, emphasis added). In this light, it is clear that one skilled in the art would understand the term "analyte" to refer to a single molecule or species that is detected.

Since the term "analyte" is currently being used by Applicant in a broader sense that is contrary to its ordinary meaning, and because the term is not clearly redefined in the specification, one skilled in the art would not be reasonably apprised of the metes and bounds of the term "analyte".

21. Claims 48 and 51-52 recites the limitation "**the epitope(s) of the analyte**". There is insufficient antecedent basis for this limitation in the claim. Claims 44 and 51 refer to an analyte "comprising at least two epitopes", and also to a "first" and "second" epitope. It is not clear which epitope or epitopes "the epitope(s) of the analyte" is referring back to, and thus the reference to a third receptor that binds to "the epitope(s) of the analyte" is not clear—is the third receptor binding to the first, second, or other epitope of the analyte?

22. Claims 44-52 and 73-74 are indefinite because the term "**epitope**" is apparently being used by the claim to mean something other than its accepted meaning. The term is indefinite because the specification does not clearly redefine the term.

Claim 73 now states that "the epitopes in the sample comprise at least two different analyte-specific antigens or at least two different analyte-specific antibodies or at least one analyte-specific antigen and one analyte-specific antibody". The wording of claim 73 indicates that Applicant is apparently employing the term "epitope" to mean something other than its accepted meaning. Specifically, the claim suggests that the epitopes *include* antibodies or antigens, i.e. that antibodies or antigens are component *parts* of epitopes, while the accepted meaning is that the opposite is true (epitopes are parts of antigens). See the attached definitions for the word "epitope" downloaded from http://www.xreferplus.com/entry/5986784 and http://www.xreferplus.com/entry/2776979, which define "epitope" as a "discrete site on an antigen to which an antibody...binds" and as "The surface portion of an antigen capable of eliciting an immune response", respectively. Thus, according to the standard meaning in the art, epitopes are portions of antigens and not the other way around. As a result, the term "epitope" as it employed throughout the claims is indefinite because the specification does not clearly redefine the term.

23. Claim 74 recites the limitation "the signal generating group bound to the first or second test areas via **the at least two epitopes**". There is insufficient antecedent basis for this limitation in the claims. Claim 44 refers to "the signal generating group bound to the first or second test areas via **said analyte**". Thus, although the independent claim mentions that the signal generating group is bound via the analyte, there is no prior

mention in the claims that the signal generating group is bound via *the epitopes* of the analyte. See also the previous Office action at item 19.

Furthermore, there is ambiguity as to what epitopes are being referred to. If "the at least two epitopes" includes the "first" and "second" epitopes mentioned in claim 44, it is unclear how the signal generating group could be bound via either of these, since in the first test area, the first epitope is bound by the immobilized first receptor, and therefore would be unable to bind to the signal generating group. Similarly, in the second test area, the second epitope is bound to the immobilized second receptor, and thus could not bind signal generating group. It is unclear how the signal generating group could be bound via *both* the first and second epitopes in either one of the test areas.

Claim Rejections - 35 USC § 102

24. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

25. Claim 49 is rejected under 35 U.S.C. 102(b) as being anticipated by Fleming (US 5,149,626).

Fleming teaches a solid phase comprising a non-porous support such as microtiter plates, glass, polystyrene, or polypropylene (see the abstract; column 5, lines 11-21 and 63-68; column 8, lines 40-68). The solid phase contains one or more different antigen-specific receptors (antibodies) that are separately immobilized to separate, defined areas on the solid phase (Figure 1; column 3, line 40 to column 4, line 30).

Fleming teaches that the solid phase may be used to detect multiple antigens or analytes in a sample (see also column 3, line 62 to column 4, line 30; column 7, line 35 to column 8, line 3). An analyte may include proteins or viruses (column 5, lines 38-43).

The teaching of different antigen-specific antibodies to assay for multiple antigens in a sample anticipates the limitation of receptors binding to an analyte via different epitopes of the analyte, in that the different antigens present different epitopes. In particular, the sample containing multiple antigens and the different antigen-specific antibodies taught by Fleming anticipate the first and second receptors that bind to different "epitopes" as claimed because Applicant has not specifically defined the terms "analyte", and further because Applicant is employing the term "analyte" broadly such that it may refer not only to a single molecule but also to a mixture of multiple antigens in a sample, as in claim 73. For example, the specification indicates that the term "analyte" may refer to "a homogeneous or heterogeneous population" (p. 5; see also the Reply of 11/29/2006, p. 8-9). Thus, the mixture of different antigens taught by Fleming reads on the claimed "analyte", and the separately immobilized antibodies specific for different antigens in the sample reads on the claimed first and second receptors binding to different epitopes.

With respect to the recitation that "a single application of the sample simultaneously contacts the first and second spatially separate test areas", the examiner notes that this refers to the intended use of the claimed solid phase and has not been given patentable weight in construing the claims. If a prior art structure is capable of performing the intended use as recited in the preamble, then it meets the claim. See, e.g., In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431 (Fed. Cir. 1997). In the

instant case, the solid phase of Fleming would be capable of performing the recited intended use. For example, the solid support may be attached to a dip stick that may be incubated with a sample (see column 5, lines 63-68; column 8, lines 58-68). Immersion of the dip stick into a beaker containing the sample may be considered "simultaneous" contacting of the dip stick (and all of its attached test areas) with a "single application" of a sample.

With respect to the recitation that "wherein a positive test result obtained on one test area is sufficient for indicating the presence of the analyte in said sample", the examiner notes that this interpretive "wherein" clause does not limit the claim to a particular structure, and thus cannot be considered to limit the scope of the claim. See MPEP 2111.04. In addition, the claim language refers only to the *intended use* of the solid phase. Since the claim does not recite anything that would serve to structurally distinguish the claimed solid phase over that of Fleming, the solid phase of the reference meets the claim because it would also be capable of performing such an intended use.

26. Claims 44, 47-49, 51-52, and 73 are rejected under 35 U.S.C. 102(b) as being anticipated by Herzberg et al. (EP 0 171 150 A2).

Herzberg et al. teach a solid phase, method, and kit for simultaneous separate multiepitope detection of an analyte in a sample (see the entire document, in particular the abstract; p. 17, lines 14-17; and p. 21, lines 18-24). For example, the reference teaches detection of the "analytes" of Newcastle Disease, Whooping cough, Measles, Influenza, and Pneumonia (see especially p. 20-21) by detecting both antigens and antibodies. This is in accord with Applicant's non-standard use of the term "analyte": the

antigens and antibodies associated with each infectious disease would also be considered to represent "epitopes" of the analyte (as consistent with Applicant's use of this term as seen in claim 73), while the individual infectious diseases, e.g. pneumonia, would be considered to be "analytes". As a result of Applicant's non-standard use of the terms "analyte" and "epitope", the claim has been broadly interpreted to mean that the different "epitopes" bound by the receptors could be either different epitopes on the same antigen molecule, or alternatively, different epitopes on distinct molecules that are part of a heterogenous or homogeneous mixture that makes up the "analyte" (see also the specification at p. 5). Thus, the teaching of Herzberg et al. of detection of antigens and antibodies associated with each infectious disease reads on the detection of multiple epitopes of an analyte as claimed.

The solid phase of Herzberg et al. comprises a non-porous support in that it may be made of polystyrene, for example, which is the same material disclosed in the instant specification at p. 23. See p. 2 and p. 21-22 of Herzberg et al. The support comprises spatially separate test areas ("pre-arranged locations" or spots) (see p. 10, line 9 to p. 11, line 6; p. 25, lines 4-11; and p. 28, line 20 to p. 29, line 3; p. 46, line 17 to p. 48; and especially Figures 1 and 3). It can be seen in Figures 1 and 3 that the areas upon which the receptors (as well as the control areas) are spotted are spatially separated from each other. The areas on the support between the spots (see especially Figure 1) constitute an "inert surface" since they contain no spotted receptor and are therefore unable to bind to the analyte. The solid support may also be "blocked" in order to prevent any further binding of protein (p. 25).

A plurality of receptors are bound to the surface of the solid support at the pre-determined locations mentioned above (see p. 5, lines 10-19; p. 6, line 16 to p. 7, line 3; p. 21, line 18 to p. 22, line 20; p. 28, line 20 to p. 29, line 3). The reference further teaches that one or more of a third receptor ("labeled probe") is used that binds specifically with the analyte (that is bound on the solid support via the receptor spots) and which is bound to a signal generating group (the label) (see in particular p. 2, lines 11-25; p. 3, line 18 to p. 4, line 2; p. 5, line 21 to p. 6, line 6; p. 29, lines 6-10; claim 6 and Figure 2). The label can be, for example, radioactive, enzymatic, or fluorescent (p. 2, lines 20-25; p. 8, lines 2-20).

The reference further teaches that a single application of the sample simultaneously contacts the first and second spatially separate test areas, since the solid support may be contacted with the sample by dipping into a liquid solution of the analyte (see p. 12, line 25 to p. 13, line 7; p. 26, line 7 to p. 27, line 5).

The reference further teaches that a positive reaction at ***a*** given support location is indicative of the presence of the analyte (p. 29, lines 1-3).

With respect to claim 44, Herzberg et al. teach providing the above solid phase and contacting the solid phase with the sample, as discussed above. The reference further teaches separately determining the presence or amount of the signal generating group bound to the pre-determined locations on the support, for example, by simple observation (p. 28, line 14 to p. 29, line 3; p. 2, lines 16-20). It is noted that due to the comprising language employed, detecting signal at the first "or" second test areas as claimed would not rule out detecting signal at all locations (i.e., both the first and second locations) as in Herzberg et al.

With respect to claim 47, Herzberg et al. teach that the solid phase may comprise control areas (see for example column 11, lines 2-6; p. 27, lines 1-5; and control spots 13 in Figure 1).

With respect to claim 51-52, Herzberg et al. also teach assay kits comprising the solid phase and a detection reagent comprising one or more of a third receptor ("labeled probe") that binds specifically with the analyte and that is bound to a signal generating group (the label) (see in particular p. 2, lines 11-25; p. 3, line 18 to p. 4, line 2; p. 29, lines 6-10; claim 6 and Figure 2). The label can be, for example, radioactive, enzymatic, or fluorescent (p. 2, lines 20-25; p. 8, lines 2-20).

With respect to claim 73, Herzberg et al. teach detection of both antibodies and antigens associated with an infectious disease analyte such as Whooping cough (p. 20).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

27. Claims 49-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ekins et al. (US 5,516,635) in view of Schonbrunner (UK Patent Application Publication GB 2313 666 A).

Ekins et al. teach a solid phase ("solid support") that includes multiple test areas ("microspots") on which capture binding agents such as antibodies may be immobilized (see especially column 2, lines 6-16 and 56-60; column 5, lines 10-59). The solid phase may comprise a non-porous support (plastic or polystyrene microtitre plate; see column 7, lines 59-60; Examples 5-6). Such a support comprises an inert surface between the test areas (wells) that does not bind to the analyte or other sample components (i.e., the partitions that separate the wells of the microtiter plate), which would be immediately apparent to one skilled in the art. More generally, the areas between the microspots on the solid support would also constitute an inert surface since no immobilized material is spotted between the spots; since there are no reagents available for binding in the regions

between the microspots such regions would not bind to the analyte or sample components.

Ekins et al. further teach that different receptors may be immobilized on different microspots on the solid phase for detection of different analytes in the same or different samples (column 5, lines 28-35; column 10, lines 52-58; column 18, claim 6). The analyte may be nucleic acid, hormones, viruses, proteins, etc. (column 8, lines 17-38). See also column 1, lines 12-55; column 8, lines 14-58; column 9, lines 37-57; claims 1-14; and Examples 5-12 in particular.

With respect to claims 51-52, the solid phase may be combined together with the detection reagent in a kit (column 10, lines 17-58; and column 20, claims 15-16). Ekins et al. further teach that such a kit may include detection reagent comprising a third receptor ("developing binding material") that also binds with the analyte and is labeled with a signal-generating group, such as by adsorption or covalent binding to a latex microsphere carrying a fluorescent or enzyme label (see the abstract; column 1, lines 53-65; and columns 3-5). Alternatively, the third receptor may be biotinylated for indirect binding to an avidin-containing "universal marker" reagent (see column 4, lines 40-62; and Example 11). Either the same or different detection reagents could be used in separate determinations for each microspot ("different binding assays") (see column 5, lines 28-40; column 9, line 61 to column 10, line 4).

Thus, Ekins et al. teach solid phase substantially as claimed comprising a first analyte-specific receptor immobilized on a first test area, a second (different) receptor immobilized on a second test area. The solid phase may be included as part of a kit

containing a detection reagent comprising a third receptor that binds specifically with the analyte and that is bound directly or indirectly to a signal-generating group.

With respect to the recitation that "a single application of the sample simultaneously contacts the first and second spatially separate test areas", the examiner notes that the limitation is directed to the intended use of the claimed solid phase. The solid phase of Ekins et al. meets the claim as it would be capable of performing this intended use. For example, Ekins et al. teach that different analytes may be assayed simultaneously on the solid support in a *single operation* (column 10, lines 48-58; column 9, line 61 to column 10, line 4). Further, as Ekins et al. teach immobilizing different receptors on different microspots on the same solid support, where each microspot is on the order of 0.01 – 1 mm in diameter, the different test areas would be contacted with the sample simultaneously when it is applied, since this is the same array-type format disclosed in the instant application at p. 23. See Ekins et al. at especially column 5, lines 10-34. Even if the microspots were to be arrayed in different wells of a multi-well plate, the solid phase of Ekins et al. would nonetheless be capable of performing the recited intended use since a multi-channel pipette could be used to simultaneously fill multiple wells in a single application. Alternatively, the test areas could be simultaneously contacted by dipping entire the solid phase into a solution of the sample. Since the prior art structure of Ekins et al. is capable of performing the recited intended use, it meets the claim. See also MPEP 2111.02.

Ekins et al. differs from the claimed invention in that it fails to specifically teach that the different receptors immobilized on different test areas (microspots) may be receptors that are specific for different "epitopes" of the same "analyte".

Schonbrunner teaches an assay method for simultaneously detecting HIV antigens and HIV antibodies (the abstract; p. 1, lines 1-4). Note that due to the manner in which the terms "analyte" and "epitope" are being employed in the claims, the "analyte" in the Schonbrunner is HIV, while HIV antigens and HIV antibodies may each be considered "epitopes" (see instant claim 73). Schonbrunner teach that detecting both HIV antigens and HIV antibodies simultaneously may allow for detection of HIV in a sample at an earlier stage of infection, thereby closing the diagnostic window slightly and allowing for earlier diagnosis (p. 3, lines 20-27; p. 5, line 33 to p. 6, line 18; p. 6, lines 23-29).

Specifically, Schonbrunner teach detecting an analyte (HIV) that has at least two analyte-specific epitopes (HIV antigens including p24 and HIV antibodies) in a sample by simultaneously or sequentially contacting the sample with at least one first receptor ("antigen capture reagent") and at least two second receptors ("antibody capture reagents") (see p. 6, line 33 to p. 8, line 8) and with a detection reagent that may be specific for the analyte in a non-competitive detection assay format (p. 11, line 4 to p. 14, line 17). The two or more antibody capture reagents would also constitute first and second receptors specific for different analyte-specific epitopes as claimed, since they may be directed against antibodies with different antigenic or epitopic specificity (p. 17, lines 6-8). Schonbrunner also teaches detection of different types, groups, or subgroups of HIV (p. 8), which would also be considered to represent different epitopes.

The detection reagent of Schonbrunner comprises a receptor that binds specifically with the analyte (either the HIV antigens or antibodies) (p. 22, line 11 to p. 23, line 3). The detection reagent further comprises a signal-generating group, which may be conjugated to the receptor before or after complex formation (p. 23, line 4 to p. 25,

line 11). In a preferred embodiment the first and second receptors are bound to a solid support (p. 16, lines 14-16; p. 17, lines 9-15; p. 18, lines 10-23), which can be provided together with the detection reagent as part of a kit (p, 35, line 15 to p. 36, line 11).

Therefore, it would have been obvious to one of ordinary skill in the art to employ the solid phase and/or test kit of Ekins et al. in order to simultaneously detect HIV antigens and HIV antibodies, as taught by Schonbrunner, in order to diagnose HIV at an earlier stage of infection.

One would have a reasonable expectation of success because Ekins et al. teach that the solid phase may be used to simultaneously detect multiple analytes in a sample, which is also the purpose of the method of Schonbrunner (i.e., to simultaneously detect both HIV antigens and HIV antibodies in a sample).

One would also have a reasonable expectation of success in using the solid phase of Ekins et al. in order to detect HIV antigens and antibodies as taught by Schonbrunner because Schonbrunner also teaches that the analyte receptors for detecting HIV may be attached to the same or a different solid supports (column 18, lines 10-23) and that the particular type of solid support is not critical (p. 20, lines 9-14). Microtiter plate wells are one example of a suitable solid support in Schonbrunner (column 20, lines 9-22), which is also an embodiment of the solid phase of Ekins. As such, one would have a reasonable expectation of success in using the receptors of Schonbrunner on the solid phase of Ekins.

One would also have a reasonable expectation of success because Ekins et al. teach that the solid phase may be used to detect proteins, which are the types of "epitopes" of the analyte HIV that are detected in Schonbrunner.

With respect to the recitation that "wherein a positive test result obtained on one test area is sufficient for indicating the presence of the analyte in said sample" in claim 49, the examiner notes that this interpretive "wherein" clause refers to the intended use of the claimed product and does not limit the claim to a particular structure. Therefore, the "wherein" clause is not considered to further limit the claim and has not been given weight in construing the claims. See MPEP 2111.04. See also Texas Instruments, Inc. v. International Trade Comm., 988 F.2d 1165, 1171, 26 USPQ2d 1018, 1023 (Fed Cir. 1993) ("A 'whereby' clause that merely states the result of the limitations in the claim adds nothing to the patentability or substance of the claim.").

Furthermore, since the solid phase of Ekins et al. and Schonbrunner et al. detects the *same* analytes using a solid phase having all of the same claimed structural limitations, it would necessarily be capable of performing this recited intended use. In particular, since the solid phase of Ekins et al. and Schonbrunner detects both HIV antigens and antibodies, a positive result in either of these (i.e., detection of either HIV antigen or anti-HIV antibodies) would indicate the presence of HIV in the sample. There are no recited structural differences that would distinguish the claimed solid phase over that of the references, and therefore, the prior art structure would also be capable of performing the recited intended use.

With respect to claim 50, the microspots of Ekins et al. have a diameter of 0.01 to 1 mm (column 5, lines 10-17).

With respect to claim 52, as noted above, Ekins et al. teach a universal marker reagent such as avidin conjugated to fluorescent microspheres (column 4, lines 40-62; column 15, lines 50-58) and such microspheres may be latex (column 3, lines 58-column

4, line 9). The universal marker reagent binds to the third receptor ("developing binding material") via avidin-biotin interaction (Example 11). The reference also teaches that the third receptor may be directly labeled with a signal-generating group (e.g., microspheres or fluorescent dye) by covalent bonding (column 4, lines 40-62; column 10, lines 35-51; Example 4b). The third receptor ("developing binding material") binds specifically with "epitope(s) of the analyte" (see for example column 8, lines 34-38). Since it is not clear what "the epitope(s) of the analyte" refers back to in claims 48 and 51-52 (see rejection under 112, 2nd paragraph above), the teaching in Ekins et al. of third receptors that bind to different epitopes than those bound by the immobilized receptors reads on the claim. This teaching is also found in Schonbrunner, which teaches a detection reagent comrpising a receptor that binds specifically with the analyte (either the HIV antigens or antibodies) (p. 22, line 11 to p. 23, line 3). Since the detection reagent may be an antibody, it would necessarily bind to an epitope on these molecules. The detection reagent of Schonbrunner further comprises a signal-generating group, which may be conjugated to the receptor before or after complex formation (p. 23, line 4 to p. 25, line 11).

28. Claims 44-46, 48, and 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ekins et al. (US 5,516,635) in view of Schonbrunner (UK Patent Application Publication GB 2313 666 A) and Lancaster (US 3,568,735).

Ekins et al. teach a solid phase ("solid support"), kit, and a method of using same that includes multiple test areas ("microspots") on which capture binding agents such as antibodies may be immobilized (column 2, lines 6-16 and 56-60; column 5, lines 10-59). The solid phase may comprise a non-porous support (plastic or polystyrene microtitre

plate; see column 7, lines 59-60; Examples 5-6). Such a support comprises an inert surface between the test areas (wells) that does not bind to the analyte or other sample components (i.e., the partitions that separate the wells of the microtiter plate), which would be immediately apparent to one skilled in the art. More generally, the areas between the microspots on the solid support would constitute such an inert surface since no immobilized material is spotted between the spots; since there are no reagents available for binding in the regions between the microspots such regions would not bind to the analyte or sample components.

Ekins et al. further teach that the solid phase may be used in a method to simultaneously determine multiple analytes in the same sample by immobilizing different receptors on different microspots (column 10, lines 52-58; column 18, claim 6). The analyte may be nucleic acid, hormones, viruses, proteins, etc. (column 8, lines 17-38). Either the same or detection reagents could be used in separate determinations for each microspot ("different binding assays") (see column 5, lines 28-40; column 9, line 61 to column 10, line 4). The method includes the steps of contacting a liquid sample containing an analyte with at least two "analyte-specific components" ("binding sites") (column 1, lines 12-55; column 8, lines 14-58) with the solid phase containing an immobilized receptor that binds to the analyte via an analyte-specific component (column 9, lines 37-57; claims 1-14; and Examples 5-12 in particular). It is noted that due to the comprising language employed, detecting the presence or amount of the signal generating group at the first "or" second test areas as claimed would not rule out detecting signal at all microspot locations (i.e., at both the first and second test areas) as in Ekins et al. (see for example column 7, lines 34-43).

Ekins et al. further teach a detection reagent comprising a third receptor ("developing binding material") that also binds with the analyte and is labeled with a signal-generating group, such as by adsorption or covalent binding to a latex microsphere carrying a fluorescent or enzyme label (see the abstract; column 1, lines 53-65; columns 3-5). Thus, Ekins et al. teach a first analyte-specific receptor immobilized on a first test area, a different (second) receptor immobilized on a second test area, as well as a detection reagent comprising a third receptor that binds specifically with the analyte and that is bound to a signal-generating group. The solid phase may be combined together with the detection reagent in a kit (column 10, lines 17-58; and column 10, claims 15-16).

Ekins et al. differs from the claimed invention in that it fails to specifically teach that the different receptors immobilized on different test areas or microspots are receptors that are specific for different epitopes of the same "analyte".

Ekins et al. also do not appear to specifically teach that "a single application of the sample is contacted with the solid phase" simultaneously with the first and second test areas. Ekins et al. do teach that different analytes may be assayed simultaneously on the solid support in a *single operation* (column 10, lines 48-58; column 9, line 61 to column 10, line 4). Further, as Ekins et al. teach immobilizing different receptors on different microspots on the same solid support, where each microspot is on the order of 0.01 – 1 mm in diameter, the different test areas would seem to be contacted with the sample simultaneously when it is applied, since this is the same array-type format disclosed in the instant application (see p. 23). However, the reference does not provide a clear, specific teaching of simultaneous contact by a single application of sample.

Schonbrunner teaches an assay method for simultaneously detecting HIV antigens and HIV antibodies (the abstract; p. 1, lines 1-4). Note that due to the manner in which the terms "analyte" and "epitope" are being employed in the claims, the "analyte" in the method of Schonbrunner is HIV, while HIV antigens and HIV antibodies may each be considered "epitopes" (see instant claim 73). Schonbrunner teach that detecting both HIV antigens and HIV antibodies simultaneously may allow for detection of HIV in a sample at an earlier stage of infection, thereby closing the diagnostic window slightly and allowing for earlier diagnosis (p. 3, lines 20-27; p. 5, line 33 to p. 6, line 18; p. 6, lines 23-29).

Specifically, Schonbrunner teach detecting an analyte (HIV) that has at least two analyte-specific epitopes (HIV antigens including p24 and HIV antibodies) in a sample by simultaneously or sequentially contacting the sample with at least one first receptor ("antigen capture reagent") and at least two second receptors ("antibody capture reagents") (see p. 6, line 33 to p. 8, line 8) and with a detection reagent that may be specific for the analyte in a non-competitive detection assay format (p. 11, line 4 to p. 14, line 17). The two or more antibody capture reagents would also constitute first and second receptors specific for different analyte-specific epitopes as claimed, since they may be directed against antibodies with different antigenic or epitopic specificity (p. 17, lines 6-8). Schonbrunner also teaches detection of different types, groups, or subgroups of HIV (p. 8), which would also be considered to represent different epitopes.

In a preferred embodiment the first and second receptors are bound to a solid support (p. 16, lines 14-16; p. 17, lines 9-15; p. 18, lines 10-23), which can be provided together with the detection reagent as part of a kit (p, 35, line 15 to p. 36, line 11).

Lancaster teaches a multi-channel dispensing apparatus for pipetting small quantities of liquid into wells of a microtiter plate (see in particular the abstract and column 1). The apparatus is capable of simultaneously dispensing predetermined volumes of liquid (see column 6). The multi-channel apparatus has the advantage that it reduces time and error (column 1, lines 13-20).

Therefore, it would have been obvious to one of ordinary skill in the art to employ the solid phase and/or test kit of Ekins et al. in order to simultaneously detect HIV antigens and HIV antibodies, as taught by Schonbrunner, in order to diagnose HIV at an earlier stage of infection.

It would have been further obvious to employ the apparatus of Lancaster in order to pipette the sample into the microtiter wells of the solid phase when performing the method, thereby simultaneously contacting the test areas in a single application of the sample. One would be motivated to do this in order to reduce time and error, as taught by Lancaster. This is particularly pertinent to the method of Ekins et al. and Schonbrunner et al. because Ekins et al. teach pipetting sample into wells of the microtiter plate (see for example Example 6). One would have a reasonable expectation of success because Ekins et al. teach that different analytes may be assayed simultaneously on the solid support in a *single operation* (column 10, lines 48-58; column 9, line 61 to column 10, line 4).

One would have a reasonable expectation of success in using the solid phase of Ekins et al. in order to detect HIV antigens and antibodies as taught by Schonbrunner because Ekins et al. teach that the solid phase may be used to simultaneously detect multiple analytes in a sample, which is the purpose of the method and reagents of

Schonbrunner (i.e., to simultaneously detect both HIV antigens and HIV antibodies in a sample).

One would also have a reasonable expectation of success in using the solid phase of Ekins et al. in the method of Schonbrunner because Schonbrunner also teaches that the analyte receptors may be attached to the same or a different solid supports (column 18, lines 10-23) and that the particular type of solid support is not critical (p. 20, lines 9-14). Microtiter plate wells are one example of a suitable solid support in Schonbrunner (column 20, lines 9-22), which is also an embodiment of the solid phase of Ekins.

One would also have a reasonable expectation of success because Ekins et al. teach that the solid phase may be used to detect proteins, which are the analyte-specific components detected in Schonbrunner.

With respect to the recitation that "wherein a positive test result obtained on one test area is sufficient for indicating the presence of the analyte in said sample" as in part (c), the examiner notes that this interpretive "wherein" clause does not require any additional active method steps to be performed, but simply states a characterization or conclusion of the results of the method steps earlier recited. It also does not limit the claim to a particular structure. Therefore, the "wherein" clause is not considered to further limit the method defined by the claim and has not been given weight in construing the claims. See MPEP 2111.04. See also Texas Instruments, Inc. v. International Trade Comm., 988 F.2d 1165, 1171, 26 USPQ2d 1018, 1023 (Fed Cir. 1993) ("A 'whereby' clause that merely states the result of the limitations in the claim adds nothing to the patentability or substance of the claim."). See also Minton v. National Assoc. of Securities Dealers, Inc., 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)

("A whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.").

Furthermore, since the method and solid phase of Ekins et al. and Schonbrunner et al. detects the *same* analytes using a solid phase having all of the same claimed limitations, it would necessarily also achieve this same result. In particular, since the method and solid phase detects both HIV antigens and antibodies, a positive result in either of these (i.e., detection of either HIV antigen or anti-HIV antibodies) would indicate the presence of HIV in the sample. There are no recited structural differences that would distinguish the claimed solid phase over that of the references, and no additional method steps recited that would distinguish the claimed method over that of the references.

With respect to claim 45, Schonbrunner et al. teach detection of HIV-1 antigens and antibodies (column 8, lines 29-35 in particular).

With respect to claim 46, the microspots of Ekins et al. have a diameter of 0.01 to 1 mm (column 5, lines 10-17).

With respect to claim 47, Ekins et al. teach that the solid phase may include control areas.

With respect to claim 48, Ekins et al. teach a universal marker reagent such as avidin conjugated to fluorescent microspheres (column 4, lines 40-62; column 15, lines 50-58) and such microspheres may be latex (column 3, lines 58-column 4, line 9). The universal marker reagent binds to the third receptor ("developing binding material") via avidin-biotin interaction (Example 11). The reference also teaches that the third receptor may be directly labeled with a signal-generating group (e.g., microspheres or fluorescent

dye) by covalent bonding (column 4, lines 40-62; column 10, lines 35-51; Example 4b). The third receptor ("developing binding material") binds specifically with "epitope(s) of the analyte" (see for example column 8, lines 34-38). Since it is not clear what "the epitope(s) of the analyte" refers back to in claims 48 and 51-52 (see rejection under 112, 2nd paragraph above), the teaching in Ekins et al. of third receptors that bind to different epitopes than those bound by the immobilized receptors reads on the claims. This teaching is also found in Schonbrunner, which teaches a detection reagent comprising a receptor that binds specifically with the analyte (either the HIV antigens or antibodies) (p. 22, line 11 to p. 23, line 3). Since the detection reagent may be an antibody, it would necessarily bind to an epitope on these molecules. The detection reagent of Schonbrunner further comprises a signal-generating group, which may be conjugated to the receptor before or after complex formation (p. 23, line 4 to p. 25, line 11).

With respect to claim 73, Schonbrunner teach detection of different analyte-specific antigens (e.g., p17, p24, p2, gp120, gp41) as well as antibodies specific for these different antigens (see in particular p. 7, line 24 to p. 8, line 9).

29. Claims 47 and 74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ekins et al. in view of Schonbrunner and Lancaster as applied to claim 44 above, and further in view of O'Connor et al. (US 5627,026).

Ekins et al., Schonbrunner et al., and Lancaster are as discussed above, which teach a solid phase and assay method for multiepitope detection of HIV. However, the references fail to specifically teach that the solid phase includes a control area or that the analyte in the sample is determined via a test area-specific cut-off.

O'Connor et al. teach methods for simultaneously determining an antibody and an antigen in a sample, such as an HIV antibody and an HIV antigen (column 2, lines 27-59). In particular, O'Connor et al. teach that wells of a microtiter plate in an ELISA assay may be used as controls (columns 8-9, "ELISA test for FIV). This is done in order to determine whether the assay is valid (see in particular column 9, lines 17-25). O'Connor et al. further teach when the signal from a test area is 3 times greater than that from the negative control that the presence of the analyte may be positively determined.

Therefore, it would have been obvious to one of ordinary skill in the art to employ control areas as taught by O'Connor et al. in the solid phase of Ekins et al. in performing the method of Ekins et al., Schonbrunner et al., and Lancaster in order to determine whether the assay was valid. It would have been further obvious to employ a test area-specific cut-off value as taught by O'Connor in order to determine whether a signal from a test area was positive.

Double Patenting

30. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a

nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

31. Claims 44-52 and 73-74 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-34 of U.S. Patent No. 6,815,217. Although the conflicting claims are not identical, they are not patentably distinct from each other because US 6,815,217 also claims a solid phase comprising a first and second spatially separate test area, which comprise, respectively, first and second receptors (see claims 1 and 17 in particular). The first receptor is specific for a first analyte and the second receptor is specific for a second analyte. The analyte may be HIV antibodies, HBs antigens, and HBc antibodies (claims 18 and 30). The solid phase may also include a control area (see claim 19). The solid phase may be provided together with a third receptor capable of binding to the analyte, which receptor may include a signal generating group (see claims 19 and 34). The solid phase may be used in an assay method to detect an analyte in a sample (claims 19-33).

US 6,815,217 does not specifically recite that the second receptor binds to a different "epitope" of the analyte than the first receptor; rather, the claims recite that the second receptor specifically binds to a second analyte (see claim 17), one skilled in the art would recognize that the claims overlap in scope because the analytes detected in US 6,815,217 may be HBs antigens and HBc antibodies (see claim 18). Since HBs antigens and HBc antibodies would be considered to be different "epitopes" of the same analyte HB (Hepatitis B virus) since these are different molecules. As such, the first and second

receptors, in binding to HBs antigens and HBc antibodies, would therefore necessarily bind to different "epitopes" of HB virus. Thus, as a result of the way in which Applicant is employing the terms "analyte" and "epitopes" (as discussed above), one skilled in the art would recognize that HBs antigens and HBc antibodies are species that anticipate the genus of "epitopes" claimed in the instant application, and further that HB virus is a species that anticipates the genus of "analyte" as claimed.

Furthermore, although US 6,815,217 does not specifically recite that the solid phase comprises a "non-porous" support, it would have been obvious to one skilled in the art to employ the specification as a dictionary in order to interpret the "solid phase support" claimed for guidance in carrying out the claimed invention. In introducing the solid phase support, the specification of US 6,815,217 at column 2, lines 29-32 states that the support is preferably non-porous.

Response to Arguments

32. Applicant's arguments in the reply of 11/29/2006 have been fully considered.

33. With respect to the rejection of claims 44, 49, and 51 regarding the term "**analyte**", Applicant's arguments (see p. 8-9) have been fully considered but they are not persuasive. Applicant argues that to clearly redefine a term, Applicants are not required to specifically identify a new definition for the term, and that all that is required is that one of skill in the art recognize that a non-standard definition is intended (Reply, p. 9), to which the examiner disagrees.

Applicant's arguments that it is possible to clearly redefine a term without setting forth a definition are unpersuasive. If the definition is not a standard one, as

acknowledged by Applicant, how would one skilled in the art know the metes and bounds unless the non-standard definition is set forth in the specification? It is not enough to merely imply, as Applicants have done, that a non-standard definition is intended without clearly setting forth the non-standard definition. MPEP 2111.01 states that:

> An applicant is entitled to be his or her own lexicographer and may rebut the presumption that claim terms are to be given their ordinary and customary meaning by clearly setting forth a definition of the term that is different from its ordinary and customary meaning(s). See In re Paulsen, 30 F.3d 1475, 1480, 31 USPQ2d 1671, 1674 (Fed. Cir. 1994) (inventor may define specific terms used to describe invention, but must do so "with reasonable clarity, deliberateness, and precision" and, if done, must "set out his uncommon definition in some manner within the patent disclosure' so as to give one of ordinary skill in the art notice of the change" in meaning) (quoting Intellicall, Inc. v. Phonometrics, Inc., 952 F.2d 1384, 1387-88, 21 USPQ2d 1383, 1386 (Fed. Cir. 1992)).

As noted in the rejection, where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, *the written description must clearly redefine the claim term* and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999).

Since Applicants are using the term "analyte" in a way contrary to its ordinary meaning in the art, but have failed to clearly redefine the term in the specification, it is maintained that the metes and bounds of the term "analyte" are unclear.

34. With respect to the rejection of claim 49 under 35 USC 102(b) as being anticipated by Fleming, Applicant argues (see p. 10-11) that the reference does not disclose that a positive test result obtained in one test area is sufficient for indicating the presence of an analyte in a sample. Applicant's arguments have been fully considered but

they are not persuasive. The claim language "wherein a positive test result obtained on one test area is sufficient for indicating the presence of the analyte in said sample" does not limit the scope of the claim, as it does not limit the claim to a particular structure. Furthermore, such language refers to the *intended use* of the claimed solid phase. Since the claim does not recite anything structurally different from that of Fleming, the solid phase of Fleming would also be capable of performing the recited intended use.

35. With respect to the rejections of claims 44-46, 48-52 and 73 under 35 U.S.C. 103(a) as being unpatentable over Ekins et al. in view of Schonbrunner, it is noted that the rejections of claims 44-46, 48, and 73 have been withdrawn in favor of the rejections over Ekins, Schonbrunner, and Lancaster as set forth above in view of the amendments to claim 44 to recite that "a single application of the sample is contacted with the solid phase, and wherein the single application of the sample simultaneously contacts the first and second spatially separate test areas".

36. Regarding the rejections of claims 49-52 over Ekins et al. in view of Schonbrunner, Applicant's arguments have been fully considered but they are not persuasive. Applicant argues (see p. 11-13) that a *prima facie* case of obviousness has not been established because the references fail to teach or suggest all the elements of the amended claims. Specifically, Applicant argues that Schonbrunner does not teach that the different receptors are bound to different test areas. This argument is not found persuasive because it amounts to a piecemeal analysis of the references. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant

case, the Ekins reference was relied upon for teaching different receptors bound to different test areas.

Applicant further argues that the Office has not identified any suggestion or motivation to combine the references (see p. 12), to which the Examiner disagrees for reasons of record as set forth in the previous Office action at p. 17—specifically, one skilled in the art would be motivated to combine the references *in order to diagnose HIV at an earlier stage of infection.*

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning (p. 12), it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case, the motivation to combine the references as discussed above was not gleaned from the disclosure, but rather was identified within the references, specifically the Schonbrunner reference (see the previous Office action at p. 16-17).

In response to applicant's argument that nowhere in the reference is there any suggestion that higher sensitivity may be achieved by using the multi-component detection of Schonbrunner with the separate test areas of Ekins (p. 12), the motivation to combine the references need not be the same as Applicant's. The fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise

be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Moreover, the examiner notes that Ekins does in fact repeatedly teach that the solid phase system achieves the advantage of higher sensitivity (see for example columns 3 and 5 and column 17, line 55 to column 18, line 24).

Applicant further argues that the references do not teach that a positive test result obtained in one test area is sufficient to indicate the presence of the analyte in the sample (p. 12). However, as discussed in the rejection above, it is noted that claim scope is not limited by claim language that does not limit a claim to a particular structure (MPEP 2111.04). The limitation does not call for any structural differences that would distinguish the claimed solid phase and test kit over the prior art structure. Furthermore, this limitation is directed to the intended use of the solid phase. Since the solid phase and test kit of Ekins and Schonbrunner meets all of the structural requirements of the claims, and also may detect the same epitopes (analyte-specific antibodies or analyte-specific antigens) of the same analyte (HIV), it would also be capable of performing the recited intended use since detection of either HIV antigen (in one test area) or of HIV antibody (in another test area) would each indicate the presence of the HIV analyte.

37. With respect to the rejections of claims 47 and 74 under 35 USC 103(a) as being unpatentable over Ekins in view of Schonbrunner, and further in view of O'Conner et al. (now rejected over Ekins, Schonbrunner, Lancaster, and O'Conner), Applicant argues as above that the references do not teach that a positive test result in one area is indicative of the presence of the analyte (p. 13), which argument is addressed immediately above. Applicant further argues as above that the Office has failed to point out any motivation or

suggestion to combine Ekins with Schonbrunner, which argument is also addressed above.

Applicant further argues that nothing in the references suggests the desirability of combining the teaching of control areas in O'Conner et al. with the teachings of Ekins and Schonbrunner, to which the Examiner disagrees for reasons of record as set forth in the previous Office action at p. 19. Specifically, O'Conner et al. teach that the use of control areas allow for positive determination of the presence of the analyte over background. Furthermore, the use of controls is not a new concept, but rather represents knowledge that was generally available to one of ordinary skill in the art, being a basic tenet of the scientific method. See also Croxson et al., of record. Since the motivation to combine the teachings of O'Conner et al. with those of Ekins and Schonbrunner was found within the cited references (and may additionally be found in the knowledge generally available to one of ordinary skill in the art), Applicant's arguments regarding hindsight reasoning are unpersuasive.

38. With respect to the rejections of claims 44-52 and 73-74 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over US 6,815,217, Applicant argues (see p. 14) that the subjects of the patent and the present application are different in that US 6,815,217 concerns the use of control spots, while the present invention relates to multiepitope analysis. This is not found persuasive because the general allegation that the instant application is "basically different" fails to establish that the claims are patentably distinct. Applicant has not specifically pointed out how the language of the claims patentably distinguishes them from those of the instant application. The fact that US 6,815,217 may related to a different general concept is not

relevant, since the claims therein are not patentably distinct from those of the instant application for reasons of record.

Conclusion

39. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 8:30-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached at (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CFoster

Christine Foster, Ph.D.
Patent Examiner
Art Unit 1641

LONG V. LE 02/09/07
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600